CLAIMS

We claim:

1. A composition comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38, said amino acid sequence comprising a loop region.

2. The composition of Claim 1, wherein said heterologous antigen is inserted at a position within said loop region.

3. The composition of Claim 2, wherein said position within said loop region is chosen from amino acid residues 77, 78, 81, and 82.

4. The composition of Claim 2, wherein said position within said loop region is at amino acid residue 76.

5. The composition of Claim 1, wherein said heterologous antigen is inserted at a position outside of said loop region.

6. The composition of Claim 5, wherein said position outside said loop region is chosen from amino acid residues 71, 72, 73, 74, 75, 83, 84, 85, 92, N-terminal and C-terminal.

7. The composition of Claim 5, wherein said position outside said loop region is at amino acid residue 44.

8. The composition of Claim 1, wherein said heterologous antigen is inserted at a position within said loop region, and in a position outside said loop region.

9. The composition of Claim 1, wherein said heterologous antigen is conjugated to said amino acid sequence.

10. The composition of Claim 1, wherein said heterologous antigen comprises at least one B cell epitope.

11. The composition of Claim 1, wherein said heterologous antigen comprises at least one T helper cell epitope.

12. The composition of Claim 1, wherein said amino acid sequence further comprises from 1 to 100 amino acids at the carboxy end of residue I^{149}.

13. The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from R^{150}, C^{150}, K^{150}, A^{150}, $R^{150}R^{151}C^{152}$, and SEQ ID NOS:2-20.

14. The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from SEQ ID NOS:22-36.

15. The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from SEQ ID NOS:42-56.

16. The composition of Claim 1, wherein said amino acid sequence further comprises at least one immune enhancer sequence.

17. The composition of Claim 1, further comprising woodchuck hepatitis virus core antigen chosen from wild type woodchuck hepatitis virus core antigen and modified woodchuck hepatitis virus core antigen lacking a heterologous antigen.

18. A nucleic acid sequence encoding said heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38 of Claim 1.

19. An expression vector comprising the nucleic acid sequence of Claim 18.

20. A composition comprising the amino acid sequence set forth in SEQ ID NO:38, said amino acid sequence comprising a loop region.

21. A method, comprising:

a) providing:

i) a mammalian subject; and

ii) a composition comprising one or more of a polypeptide comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38, said amino acid sequence comprising a loop region, and an expression vector encoding said polypeptide; and

b) administering said composition to said subject under conditions such that an immune response is generated.

22. The method of Claim 21, wherein said immune response comprises one or more of lymphocyte proliferative response, cytokine response and antibody response.

23. The method of Claim 22, wherein said antibody response comprises production of IgG antibodies.

24. The method of Claim 23, wherein said IgG antibodies comprise an autoantibody.

25. A method for producing an immunogenic composition, comprising:

a) providing:

i) a heterologous antigen; and

ii) a hepatitis virus core antigen;

b) altering at least one of said heterologous antigen and said hepatitis virus core antigen, with a modification chosen from insertion of at least one acidic amino acid residue and substitution of at least one acidic amino acid residue; and

c) inserting said heterologous antigen of step b within said hepatitis virus core antigen of step b, to produce a modified hepatitis virus core antigen;

d) expressing said modified hepatitis virus core antigen under conditions suitable for producing particles having a diameter of 25 to 35 nm.

26. The method of Claim 25, wherein in the absence of said altering, expression of said modified hepatitis virus core antigen yields 25 fold less particles than does expression of a wild type hepatitis virus core antigen.

27. The method of Claim 25, wherein said at least one acidic amino acid residue comprises at least one aspartic acid residue and at least one glutamic acid residue.

28. The method of Claim 25, wherein said insertion is in at least one position chosen from the N-terminus and the C-terminus of said heterologous antigen.

29. The method of Claim 25, wherein said substitution comprises a replacement of at least one non-acidic amino acid residue within said heterologous antigen, with said at least one acidic amino acid residue.

30. The method of Claim 25, wherein said altering produces a modified heterologous antigen with an isoelectric point in the range of 3.0 to 6.0.

31. The method of Claim 30, wherein said hepatitis virus core antigen is a woodchuck hepatitis virus core antigen.

32. A composition comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:40, said amino acid sequence comprising a loop region.

33. A composition comprising the amino acid sequence set forth in SEQ ID NO:40, said amino acid sequence comprising a loop region.

34. A method, comprising:

a) providing:

i) a mammalian subject; and

ii) a composition comprising one or more of a polypeptide comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:40, said amino acid sequence comprising a loop region, and an expression vector encoding said polypeptide; and

b) administering said composition to said subject under conditions such that an immune response is generated.

35. A method for producing an immunogenic composition, comprising:

a) providing:

i) a heterologous antigen; and

ii) a ground squirrel hepatitis virus core antigen;

b) altering at least one of said heterologous antigen and said ground squirrel hepatitis virus core antigen, with a modification chosen from insertion of at least one acidic amino acid residue and substitution of at least one acidic amino acid residue; and

c) inserting said heterologous antigen of step b within said ground squirrel hepatitis virus core antigen of step b, to produce a modified ground squirrel hepatitis virus core antigen;

d) expressing said modified ground squirrel hepatitis virus core antigen under conditions suitable for producing particles having a diameter of 25 to 35 nm.